SUPPORT FOR THE AMENDMENTS

Claims 11-14, 16-19, and 26 have been amended been amended for clarity. Accordingly, support for amended Claims 11, 19, and 26 can be found in the same claims, as previously presented.

No new matter has been added. Claims 11-14, 16-19, 21-26, 28-32, 35-46, 48, and 49 remain pending in the present application.

REMARKS

Present Claims 11-14 and 16-18 relate to aerosol formulations which comprise budesonide, a propellant vehicle, and an antioxidant, wherein the budesonide is completely dissolved in the propellant vehicle and said propellant consists of one or more hydrofluroralkanes and a cosolvent.

Present Claims 19, 21-25, and 35-46 relate to pressurized metered dose inhalers which comprising a container equipped with a metering valve and which contain such an aerosol formulation. Present Claims 26, 28-32, 48, and 49 relate to methods for the treatment of a bronchial disorder in a subject in need thereof comprising administering to said subject such an aerosol formulation.

Thus, all of the present claims explicitly require the presence of a formulation which contains budesonide and that the budesonide be completely dissolved.

The cited references contain no disclosure or suggestion of the presently claimed aerosol formulations, pressurized metered dose inhalers, or methods. Accordingly, these references cannot affect the patentability of the present claims.

The rejection of Claims 11-14, 16-19, 21-26, 28-32, 39-46, 48, and 49 under 35 U.S.C. §103(a) over U.S. Patent No. 6,129,905 (Cutie) in view of U.S. Patent No. 5,776,433 (Tzou et al.) is respectfully traversed.

On page 6 of the Office Action, the position is taken that Cutie "teaches solutions of active agents such as budesonide, cosolvents such as ethanol, propellants such as HFA 134a and excipeints such as antioxidants." However, this assertion is simply incorrect.

It is true that in the section entitled Background of the Invention, Cutie discloses a wide variety of aerosol formulations for oral inhalation, including dry-powder formulations, solutions, suspensions, and combination slurry-solutions (See, col. 1, line 24, to col. 3, line 12). However, Cutie does not disclose that any of the formulations discussed in the Background section contain budesonide.

The only time Cutie mentions budesonide is in connection with formulations, which are clearly not solutions. Specifically, the only mention of budesonide in Cutie is in connection with the "inventive" formulations:

> Drugs which may be administered via the ***inventive formulations*** include: flunisolide, flunisolide hemihydrate, cromolyn sodium, isoproterenol sulfate, metaproterenol sulfate, ipratropium bromide, terbutaline sulfate, beclomethasone, beclomethasone dipropionate, beclomethasone monopropionate, albuterol, dexamethasone, dexamethasone sodium phosphate, isoproterenol HCl, phenylephrine bitartrate, epinephrine, epinephrine bitartrate, ergotamine tartrate, triamcinolone acetonide, ***budesonide***, fluticoside, salmeterol xinafoate, perbuterol sulfate, and pharmaceutically acceptable salts and derivatives of any of these drugs.

Cutie, col. 4, lines 24-36, emphasis added.

The fact that the inventive formulations of Cutie are dispersions, not solutions, is made abundantly clear in the very first sentence of the section entitled Detailed Description of the Invention:

> The present invention provides an aerosol formulation for mucosal or topical administration comprising a therapeutically effective amount of at least one drug

> (active), a sugar and optionally one or more pharmaceutically acceptable excipients, ***dispersed*** in a pharmaceutically acceptable propellant or mixture of such propellants.

Cutie, col. 3, lines 46-51, emphasis added.

This understanding is reinforced by the disclosure of the role of the sugar:

> The sugar is capable of (1) facilitating the dispersion of the drug(s) and/or excipients; (2) stabilizing formulations, either physically, chemically, or both; (3) facilitating the transfer of aerosolized drug; (4) facilitating the drug's micronization and/or deaggregation or manipulating other in vitro qualities of the drug or formulation containing the same; (5) acting as a respiratory sensitizer or desensitizer of drug surface interactions at topical and/or mucosal surfaces; and (6) acting as a density modifier.

Cutie, col. 4, lines 16-24.

In addition, Cutie makes it clear that both the sugar and the active agent remain in solid form in the formulation right up to administration:

> The particle size of the sugar should be no greater than 10 microns diameter, since larger particles are not transported to the airways effectively. Preferably substantially all of the particles should be less than 5 microns in diameter. Most preferably substantially all of the particles should be less than about 2 microns in diameter. There is no lower limit on particle size except that which will be readily absorbed and retained on or in body tissues. When particles of less than about one-half micron in diameter are administered by inhalation, they tend to be exhaled by the patient.

Cutie, col. 4, line 62, col. 5, line 4.

> The particle size of the micronized drug should be no greater than 100 microns in diameter, since larger particles may clog the value or orifice of the container. Preferably, substantially all of the particles should be less than 25 microns in diameter. More preferably, substantially all of the particles should be less than about 10 microns in diameter. Most preferably, substantially all of the particles should be from about 0.5 to about 8 microns in diameter.

Cutie, col. 5, lines 11-17.

As can be seen, Cutie does not disclose any formulations in which budesonide is completely dissolved in the propellant. Instead, this reference only discloses dispersion formulations.

Applicants respectfully submit that there is nothing in Tzou et al. which can cure this basic deficiency of Cutie. Quite simply, Tzou et al. is completely silent in regard to budesonide. Instead, Tzou et al. only discloses aerosol compositions comprising flunisolide, ethanol and HFA propellants. Again, no reference is made in this reference of budesonide.

Thus, even the combined teachings of Cutie and Tzou et al. fail to disclose or suggest any aerosol formulation in which budesonide is dissolved in a propellant. In fact, from the teachings of Cutie and Tzou et al., one of skill in the art would have no motivation for even attempting to prepare an aerosol formulation in which budesonide is dissolved in a propellant or have any expectation of success that it would be possible to prepare such a formulation.

For this simple reason, even the combined teachings of Cutie and Tzou et al. cannot make a *prima facie* case of obviousness against the present claims.

Accordingly, the rejection is improper and should be withdrawn, for this reason alone.

The rejection of Claims 35-38 under 35 U.S.C. §103(a) in view of Cutie in view of Tzou et al. and further in view of U.S. Patent No. 6,558,651 (Riebe et al.) is respectfully traversed. As explained above, even the combined teachings of fail to disclose or suggest any aerosol formulation in which budesonide is dissolved in a propellant. There is nothing in Riebe et al. which can make up this shortcoming.

Riebe et al. discloses the use of a recrystallised form of salbutamol sulphate to reduce or eliminate the problem of drug *adhesion or deposition* to the inner surfaces of the MDI. Thus, Riebe et al. is directed toward powder formulation, not a formulation in which the active agent is dissolved in the propellant.

For this simple reason, even the combined teachings of Cutie, Tzou et al., and Riebe et al. cannot make a *prima facie* case of obviousness against the present claims.

Moreover, it is important to note that Riebe et al. deals only with the specific problem of the adhesion of ***particulate*** salbutamol to the walls of the can. There would be no reason for the skilled in the art to turn to Riebe et al. to solve the problem of the addressed by the present claims, *i.e.*, chemical degradation of budesonide which is in ***solution***. Simply put, the problem of ***adhesion of a particulate*** drug does not exist in the case of the presently claimed metered dose inhalers, because the budesonide is dissolved and does not exist as a particulate drug.

For all of these reasons, the rejection is improper and should be withdrawn.

The provisional rejection of Claims 11-14, 16-19, 21-26, 28-32, 35-46, 48, and 49 for obviousness-type double patenting in view of claims 1-13 of U.S. Patent Application Serial No. 10/244,519, now U.S. Patent No. 7,223,381 ("the '381 patent") is respectfully traversed. As noted above, all of the pending claims require the presence of an antioxidant. Quite simply, there is nothing in any of the claims of the '381 patent which would suggest an aerosol formulation which contains an antioxidant.

Accordingly, the rejection is improper and should be withdrawn.

Applicants respectfully submit that the above-identified application is now in condition for allowance, and early notice of such action is earnestly solicited.

Respectfully submitted,

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